IN THE UNITED STATES DISTRICT COURT FOR THE
MIDDLE DISTRICT OF TENNESSEE
NASHVILLE DIVISION

RUTH SMITH, Individually and as Widow for the Use and Benefit of Herself and the Next Kin of Richard Smith, Deceased,	)	
Plaintiff,	)	Civil No. 3:05-0444
	)	Judge Aleta A. Trauger
v.	)	(Dist. Of MA No. 1:05-cv-11515PBS)
PFIZER, INC., *et al.*,	)	
Defendants.	)	

JOINT PRE-TRIAL ORDER

Pursuant to Federal Rule of Civil Procedure 16 and this Court's December 10, 2009 Order Setting Case for Trial (R. 38), the Parties submit this Joint Pre-Trial Pre-Trial Order.

I. Parties

The Plaintiff is Ruth Smith ("Plaintiff"), who brings this action individually and as widow of decedent Richard Smith ("Decedent") for the use and benefit of herself and the next kin of the Decedent. The Defendants are Pfizer Inc and Warner-Lambert Company LLC (collectively, "Pfizer" or "Defendants").

II. Pleadings

The pleadings in this case are amended to conform to this Order and this Order supplants those pleadings.

III. Jurisdiction

This Court has diversity jurisdiction over all remaining claims in the case pursuant to 28 U.S.C. § 1332. There is complete diversity among the parties and the amount in controversy exceeds $75,000, exclusive of interests and costs.

IV. Parties' Theories of the Case

A. Plaintiff

This is a wrongful death case arising out of the death of Richard Smith. Plaintiff alleges that Richard Smith died by suicide after taking the prescription medication Neurontin, also known as gabapentin, which is manufactured and marketed by the Defendants. Plaintiff will offer evidence to show that taking gabapentin causes an increased risk of suicidality in some patients; that Defendants were negligent and failed to disclose this risk to Richard Smith and his prescribing physicians and medical providers; that Defendants misrepresented information known to the defendants and suppressed or concealed material facts about gabapentin's capacity to cause depression and suicidality; and that Defendants did not take reasonable and necessary steps to investigate, research and disclose the risks of suicidality with Neurontin after it came on the market.

The Defendants are Pfizer, Parke-Davis, and Warner-Lambert, formerly a subsidiary of Parke-Davis. Parke-Davis and Warner-Lambert originally submitted Neurontin – gabapentin --- for FDA approval and marketed Neurontin-gabapentin. Pfizer bought Parke-Davis and Warner-Lambert in 2000. In addition to its own conduct, Pfizer is responsible for the acts of Parke-Davis and Warner-Lambert.

Parke-Davis filed its New Drug Application for Neurontin solely for add-on therapy for epilepsy and not for any other illness, disease, or medical indication. When Parke Davis filed the Neurontin (gabapentin) New Drug Application with the FDA, as part of its submission, Parke-Davis submitted data documenting patient adverse events observed and reported in its own clinical trials. In the total exposed population of patients in the New Drug Application for Neurontin submitted to FDA in 1992, seventy-eight, or 5.3 percent, of the reported adverse events were of depression, including nineteen instances where the patient had no prior history of depression, twenty-two instances where the patient required treatment for his or her depression, and nine instances where the patient had to withdraw from the study due to depression. The seventy-eight "serious" adverse events identified included seven reports of depression involving suicidal ideation, six of drug overdoses, and two suicide attempts. Six of the seventy-eight "serious" adverse events, including the two suicide attempts, were deemed by the Defendants' own clinical investigator to be "possibly or probably" related to gabapentin. There were also numerous mood and behavioral disturbances, or "psychobiologic" adverse events, reported in the studies.

Defendants' clinical trials reported within the New Drug Application included a report of a positive dechallenge/rechallenge event where the patient experienced severe depression and suicidal ideation while on gabapentin that resolved when he was taken off the drug and that re-appeared when the patient was given gabapentin again.

The FDA, in 1992-1993, as part of a medical-statistical review of the Defendant's New Drug Application for Neurontin, noted five "serious events", including depression, which could "limit the drug's widespread usefulness." Specifically, FDA stated that "depression, while it may not be an infrequent occurrence in the epileptic population, may become worse and require intervention or lead to suicide, as it has resulted in some suicidal attempts." The FDA stated that

in Defendants' clinical database of 2048 patients, gabapentin had a risk profile that was uncertain, with five groups of important adverse events that had not yet been fully characterized, including clinically important depression. The FDA also commented at that time about dropouts in the clinical trials and gabapentin's lack of sustained efficacy; the FDA stated the following: "Accumulated long range safety data are limited by the excessive attrition due to apparent lack of sustained efficacy."

Defendants had specific knowledge that Neurontin may contribute to depression and suicidality from clinical studies and trials conducted as part of this New Drug Application in 1992. Parke Davis and Warner Lambert had specific knowledge of the FDA's medical-statistical review regarding Neurontin. On or about December 7, 1992, Dr. Richard Spivey, then Senior Director of Regulatory Affairs at Parke Davis, obtained the FDA review from the FDA. Dr. Spivey provided the review to Janeth Turner, Parke-Davis' Director of Regulatory Affairs employee. On December 7, 1992, Ms. Turner provided the FDA Review to Dr. Mark Pierce, Parke Davis's Vice President of Clinical Research, and Mr. Mickey Fletcher, who reported directly to the Parke Davis Vice President of Drug Development. Between December 7, 1992 and December 9, 1992, Dr. Spivey, Ms. Turner, Dr. Pierce and Mr. Fletcher read and became aware of the 1992 FDA Review.

Defendants' employee Janeth Turner also was a member of Defendants' Drug Development Team and New Product Committee whose stated purpose was to explore new uses for Neurontin beyond the epileptic population. At no time did Defendants' employee Ms. Turner communicate to any other member of Defendants' Development Team, or New Product Committee, the FDA's concern that "[l]ess common but more serious events may limit the drugs [Neurontin's] widespread usefulness…depression, while it may not be an infrequent occurrence in the epileptic population, may become worse and require intervention or lead to suicide, as it has resulted in some suicidal attempts."

On or about December 15, 1992, the Peripheral and Central Nervous System Drugs Advisory Committee to the Department of Health and Human Services voted to recommend Neurontin for one very specific use in a limited population: the adjunctive treatment for refractory epilepsy. Approximately one year later, on December 30, 1993, the company received FDA approval to market Neurontin only for the adjunctive treatment of epilepsy in adults. The FDA stated that the drug is only effective at 900 to 1800 milligrams per day.

Defendants later sought approval from the FDA for additional prescription uses for Neurontin. Defendants' application to the FDA for approval of Neurontin as a monotherapy for partial seizures was denied on August 26, 1997.

Beginning in 1995, Defendants Parke-Davis and Warner Lambert engaged in a multi-faceted marketing strategy designed to increase sales of Neurontin for uses not approved by the FDA. Such uses are known as "off-label" uses. Defendants began to illegally market and promote the sale of Neurontin for "off-label uses" which were not approved by the FDA, such as the treatment of pain, bipolar disorder and anxiety. The illegal marketing and promotion included: a) sales representatives detailing Neurontin to prescribing physicians for those "off-label" uses and at higher doses than had been tested or approved; b) funding presentations by consultants and liaisons to encourage word-of-mouth recommendations for off-label uses within

the medical community; c) increasing clinical testing and development for new unapproved (off-label) uses for Neurontin; d) affirmative promotional statements intended to conceal or misrepresent negative or contradictory data on the Neurontin's safety or efficacy for unapproved, off-label uses, and e), placing articles in publications to be read by doctors that stated that Neurontin was observed to improve patients who had been treated with Neurontin for "off-label" psychiatric and pain uses.

Clinical evidence from Defendants' studies did not support Defendants' promotion of Neurontin as safe and effective for off-label uses. However, Defendants and their representatives promoted off-label uses even where there was contradictory clinical evidence of its efficacy. Defendants' marketing campaign for Neurontin correlates with a substantial rise in Neurontin sales for off-label uses. Sales of Neurontin for non-FDA approved (off-label) uses have skyrocketed steadily since 1998. From 2000 to 2004, off-label usage constituted 93 to 94 percent off all Neurontin sales. This sharply contrasts with sales for approved uses where sales have declined during the relevant period.

Defendants sponsored a study in 1998, which concluded that patients receiving Neurontin did worse than those patients on placebo sugar pills. Although Defendants were aware of the results of this study, they did not publish the study's results until 2000, after a significant number of physicians were induced to prescribe Neurontin.

From the time that Defendants began to market Neurontin to the public in 1993 through the time that Richard Smith committed suicide on May 13, 2004, Defendants did not disclose or warn that Neurontin may cause psychobiologic events including depression and suicidality, and Defendants did not disclose or warn that Neurontin increased the risk of suicidality.

Defendants' marketing strategy through at least May 2004, before Richard Smith's death, was to compare and set apart Neurontin from competing drugs, such as Keppra, that already had a specific warning related to suicide.

As of May 2004, without FDA approval of Neurontin for indications beyond epilepsy, the law prohibited Defendants from marketing or promoting Neurontin for any other ("off label") uses.

However, the sale of the drug Neurontin was introduced by Defendants in interstate commerce for unapproved uses and without prior FDA approval. The sale of the drug Neurontin was introduced by Defendants in interstate commerce for unapproved uses without adequate directions being provided to physicians and consumers for such uses.

Warner-Lambert Company distributed Neurontin as an unapproved new drug, beginning as early as about April of 1995, and continuing thereafter until at least in or about August 20 of 1996 in the Middle District of Tennessee and elsewhere. Warner-Lambert Company distributed Neurontin as a misbranded drug, beginning as early as in or about April of 1995, and continuing thereafter until at least in or about August 20 of 1996 in the Middle District of Tennessee and elsewhere.

Dr. David Franklin was employed by Parke-Davis in 1996 as a medical liaison. He commenced a whistle-blower lawsuit in 1997 which exposed Defendants' national campaign of

illegal marketing and promotion of Neurontin off-label for unapproved uses. Dr. Franklin was trained by Parke-Davis to engage in the illegal promotion of Neurontin for unapproved uses at training courses that Parke-Davis medical representatives and sales representatives were required to attend. Dr. Franklin was trained to promote Neurontin for a variety of uses that had not been approval by the FDA. To that end, false information regarding clinical trials was routinely given to physicians, and negative information about the drug's effectiveness for bipolar disorder and pain was suppressed. Dr. Franklin's job was to proactively increase sales of Neurontin for off-label uses. Physicians who transitioned from prescribing other drugs to Neurontin were rewarded with consulting fees. Pfizer was aware of Dr Franklin's allegations in 2000 when it bought Parke-Davis and Warner-Lambert.

Defendant Warner-Lambert Company LLC was charged in the United States District Court for the District of Massachusetts with improper off-label marketing in violation of 21 U.S.C. §§ 331(a), 331(d), 333 (a)(2), 352 (f)(10) and 355 (a). Defendant Warner-Lambert Company LLC pled guilty to the charges on June 7, 2004. As part of its guilty plea in 2004, Defendants admitted that the Neurontin label provided inadequate directions for use.

Defendant Warner-Lambert Company, LLC, as part of the guilty plea, was ordered to pay a criminal fine of 240 million dollars.

At all times before Richard Smith's death, Defendants considered the term "suicide" to be an unlabeled adverse event, meaning an event that is not specifically identified in the label to warn or alert prescribing doctors of a known or expected side effect reported with the drug. Defendants submitted reports of suicide to the FDA as unlabeled adverse events on a 15-day expedited basis.

However, after Richard Smith's death, on December 21, 2005, Defendants submitted a labeling change to the FDA in which "suicide" would be added to the label. On May 3, 2006, FDA approved the labeling change. Thereafter, Defendants considered "suicide" to be a labeled event and transmitted to the FDA reports of "suicide" as labeled adverse events on its periodic reports.

On January 31, 2008, the FDA issued an Alert to healthcare professionals stating that: "[P]atients receiving antiepileptic drugs had approximately twice the risk of suicidal behavior or ideation…compared to patients receiving placebo." Neurontin is one of the eleven anti-epileptic drugs identified in the FDA Alert. The Alert reported that the increased risk of suicidal behavior or ideation was statistically significant and noted that "[f]our of the patients who were taking one of the antiepileptic drugs committed suicide, whereas none of the patients in the placebo group did." The Alert advised that all patients treated with AEDs (antiepileptic drugs) should be monitored closely for depression and suicidality and other unusual changes in behavior, explaining that "symptoms such as anxiety, agitation, hostility, mania and hypomania may be precursors to emerging suicidality."

In May 2008, the FDA issued a statistical review that concluded that "antiepileptic drugs are associated with increased risk of suicidality relative to placebo in randomized placebo-controlled trials." The FDA placed gabapentin in the ABAergic/GABAmimetic drug group, the

drug group that demonstrated a statistically significant association with increased risk of suicidal behavior or ideation.

On July 10, 2008, Dr. Russell Katz, the FDA Director of the Division of Neurology Products, stated on the record that the FDA study established causality between antiepileptic drugs and suicidality. The FDA study supports an association between Neurontin and suicidality. Neurontin increases the risk of suicidal thoughts or behavior in patients taking Neurontin for any indication. There is an association between Neurontin and an increased risk of suicidality.

On December 16, 2008, the FDA required all manufacturers of antiepileptic/ anticonvulsant drugs to include a warning in their labeling and to inform patients of the risks of suicidal thoughts and actions. Neurontin's labeling as of April 2009 includes language that "Antiepileptic drugs (AEDs), including Neurontin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication."

Gabapentin is a GABAergic drug. GABAergic drugs have the capacity to contribute to negative effects on mood and behavior. GABA is the primary inhibitory neurotransmitter in the brain and spinal cord. Developed as an antiepileptic compound, gabapentin was originally conceived to be similar in chemical structure and therefore in function to GABA. Many antiepileptic drugs were designed to counteract the over-excitation in an epileptic's brain by increasing the amount of GABA in the brain. Such drugs are often referred to as "GABAergic". The FDA has documented a statistically significant association between GABAergic antiepileptic drugs and increased risk of suicide. Gabapentin has been presented by Defendants as a GABAergic drug. Defendants designed gabapentin as a GABAergic drug. Gabapentin has been shown to prompt an increase in whole-tissue brain concentrations of GABA. The presence of GABA in the nuclei where serotonin originates (the raphe nuclei) reduces the rate of serotonin release. Studies of Neurontin have also showed that a specific and high-affinity binding site for Neurontin may be the auxiliary alpha-2-delta protein subunit of voltage-gated calcium channels in the brain.

Several animal studies have demonstrated that gabapentin decreases monoamine neurotransmitter (i.e., serotonin, norepinephrine and dopamine) release in vitro (experiments on cell and tissue cultures). Gabapentin has been shown to reduce the release of monoamine neurotransmitters under laboratory conditions. The decrease of serotonin and other monoamines in the brain is deleterious to mood, including depression and aggression. There is a causal relationship between low levels of serotonin in the brain and depression and suicide. Depression is associated with serotonin depletion in many people. By altering the brain chemistry of its users, Neurontin has the biological capacity to cause mood and behavioral changes that contribute to suicidality.

Neurontin increases the amount of GABA (gamma-aminobutyric acid), a neurotransmitter, in the brain. This increase of GABA leads to a decrease of other neurotransmitters in the brain, like serotonin, norepinephrine and dopamine. The decrease in serotonin and norepinephrine can prompt behavioral disturbances, depression, and suicidal behavior. Neurontin's "alpha-2-delta" mechanism of action results in the decrease of these neurotransmitters.

Plaintiff will offer evidence that Defendants' conduct was a substantial factor, also called a proximate cause, of Richard Smith's injuries and death. Plaintiff will offer evidence to show that Richard Smith's death resulted in damages to his family, including loss of consortium, guidance and services, and that they are entitled to compensatory and punitive damages because of Defendants' conduct.

Prior to Mr. Smith's death, Defendants promoted Neurontin to his physicians and health care providers via direct sales representative detail visits to his doctors' offices. Before prescribing Neurontin to Mr. Smith, fellow physicians who specialized in pain management at Dr. Edward Mackey's practice were visited by a Parke-Davis Warner-Lambert sales representatives, at which time they promoted the use of Neurontin. Dr. Mackey, an orthopedic surgeon, testified that it is more likely than not that Pfizer, Parke-Davis, Warner-Lambert sales representatives came and talked to him to promote the use of Neurontin. Defendants' sales representatives visited Pamela Krancer, an advanced practice nurse, and promoted the use of Neurontin. Pfizer acknowledges it was inappropriate to have their sales representatives promote Neurontin to physicians other than neurologists and epilepsy doctors regarding Neurontin.

When Dr. Mackey and/or his partners were visited by Parke-Davis Warner-Lambert sales representatives before Dr. Mackey's prescription of Neurontin to Mr. Smith, the defendants' sales representatives discussed the use of Neurontin for the treatment of neuropathic pain. The sales representatives did not ever disclose to Dr. Mackey or his partners any information whatsoever about whether Neurontin could increase the risk of suicidal behavior in people taking Neurontin. As part of his job as a prescribing physician, Dr. Mackey relied on the information imparted to by the sales representatives to his partners, who specialized in pain management.

Dr. Mackey treated Mr. Smith during the approximately one month period from February 12, 2004 until March 9, 2004. On March 9, 2004, Dr. Mackey prescribed Neurontin for Mr. Smith. Had Dr. Mackey been told by Defendants that Neurontin usage increased the risk of depression and/or suicidality, he probably would have changed the way he treated Richard Smith. Had Dr. Mackey known of these problems associated with Neurontin, he would have given Richard Smith specific warnings and told him to be observant about side effects. Nurse Krancer prescribed Neurontin for Mr. Smith in March 2004. She testified that drug representatives typically detailed her in her job as a nurse. It is important to her that the representative be honest and forthright and that they tell her the good and the bad as she does take into account what the representatives tell her. Had Nurse Krancer been told by Defendants that Neurontin was associated with increases in depression and suicide, she would have educated her patients, including Mr. Smith, regarding these potential side effects. She thinks that people have a right to know what medications might do to them; the side effects and interactions with other medications.

Paul McCombs III is a neurological surgeon who treated Mr. Smith for radiating leg pain. Dr. McCombs re-filled a prescription for Neurontin that was initially prescribed by Dr. Mackey. Dr. McCombs prescribed Neurontin for Mr. Smith on March 24, 2004. Dr. McCombs stated that is would be important for him to know if suicide or depression is considered a prominent side effect of the drug. Had Dr. McCombs been informed by Defendants' representatives who were talking to him about Neurontin that the drug was associated with depression, he would have reviewed the medication options, and he would have been very careful with it if he still decided

to prescribe it. He would have given Mr. Smith and his family some significant warnings and would have made sure they were aware that if his depression seemed to be getting worse, he needed to contact someone.

Dr. Mackey, Dr. McCombs and Nurse Krancer prescribed Neurontin to Mr. Smith for neuropathic pain which is an off-label use.

Defendants' sales representatives never disclosed to Dr. Mackey, Dr. McCombs or Nurse Krancer that suicidality is a risk with Neurontin. Defendants did not disclose to Mr. Smith's prescribing medical providers that Neurontin usage was associated with depression and/or suicidality. Defendants did not disclose to Mr. Smith's prescribing medical providers that Neurontin usage increased the risk of depression and/or suicidality. Defendants did not disclose to Mr. Smith's prescribing medical providers that the FDA, in 1992, was concerned that Neurontin usage may worsen depression or lead to suicide attempts. Defendants did not disclose to Mr. Smith's prescribing medical providers that Neurontin could increase the risk for suicidality in patients who were already pre-disposed or susceptible to committing suicide.

When Richard Smith took Neurontin, Defendants' labeling for Neurontin did not include any warning for Suicidal Behavior. When Richard Smith took Neurontin, Defendants' labeling for Neurontin did not include language that Neurontin increases the risk of suicidal thoughts or behavior in patients taking Neurontin for any indication.

At the time of his death on May 13, 2004, Richard Smith was employed as a service manager at Nashville Office Machines. He had 20 people under him. He went from full-time to part-time employment in March of 2004. He had been married to Ruth Smith for nearly 60 years. He had four adult daughters: Sherri Hoskins, Gayle Lawson, Cindy Charlton and Donna Caenahan. Mr. Smith had been a minister for the Church of Christ for over 50 years. He was a popular minister who counseled many members of the community in which he lived. He was a very spiritual-minded man, and was the spiritual leader of his family. Mr. Smith's death was inexplicable to the family members because Mr. Smith was a godly man and he knew suicide was wrong.

After Mr. Smith started taking Neurontin in March 2004, he became aware that Neurontin was making him feel not himself. He remarked upon this fact to several family members and at least one physician who made contemporaneous notes of these statements. Dr. Christopher Wood, the family dentist and friend who had known Mr. Smith for some twenty years stated that when he saw Mr. Smith on May 10, 2004, four days before his death, Mr. Smith told him that Neurontin was making him feel "weird". Mr. Smith's son-in-law, Wes Carnahan, who is a doctor of pharmacology, stated that on the Sunday five days prior to his death Mr. Smith asked him about certain side effects he was experiencing, and asked if Dr. Carnahan thought they could be attributed to the Neurontin he was taking. Mr. Smith told his son-in-law that he was feeling "loopy" and not himself. Dr. Carnahan replied that that was a possibility based upon his experience with other patients at the VA who were taking Neurontin and had described those same side effects to him.

On May 13, 2004, Richard Smith administered a self-inflicted gunshot wound to the head. He was pronounced dead at the scene.

B. Defendants' Theory of the Case and Affirmative Defenses

1. Defendants' Theory of the Case

Plaintiff, Ruth Smith seeks to recover damages for the death of her husband, Richard Smith. She alleges that Mr. Smith's use of Neurontin caused him to commit suicide on May 13, 2004, at the age of 79. During his life, Mr. Smith suffered from many well-established suicide risk factors, including chronic pain, depression, hopelessness, and suicidal ideation. These risks were present in his life years before he ever filled his one prescription for Neurontin. In order to recover, Plaintiff has the burden of proving (1) that Neurontin's label failed to contain adequate warnings at the time it was prescribed and ingested by Mr. Smith, and (2) that the lack of adequate warnings was both a cause-in-fact and proximate cause of Mr. Smith's death. Plaintiff will be unable to sustain her burden of proof with respect to any elements of her claim. The evidence at trial will show as follows.

Neurontin was adequately labeled. First, the evidence will show that Neurontin contained adequate warnings. On January 15, 1992, Warner-Lambert submitted to the Food and Drug Administration ("FDA") a new drug application ("NDA") seeking approval to market Neurontin for use as adjunctive therapy in the treatment of partial seizures in patients with epilepsy. In December 1992, after a careful review of the Neurontin safety data, FDA summarized its clinical data review of the initial NDA submission and multiple safety updates in a comprehensive 113-page report. The FDA evaluated all adverse events from the clinical trials to identify potential safety risks, including adverse events of depression and suicidality. In the FDA report, Dr. Cynthia McCormick, the FDA Medical Review Officer who was primarily responsible for reviewing the Neurontin clinical safety data, specifically analyzed and discussed suicide-related events in Neurontin patients. She found no evidence that Neurontin increases the risk of or causes depression or suicidal behavior. Dr. Paul Leber, Director of FDA's Neuropharmacological Division, also prepared a report of the safety and effectiveness of Neurontin, entitled, "Approval Action Memorandum," dated December 13, 1993. Dr. Leber's findings were consistent with those of Dr. McCormick.

An independent panel of outside experts, FDA's Peripheral and Central Nervous System Drugs Advisory Committee, also evaluated the data on Neurontin. Dr. McCormick's clinical review was provided to the Committee and she discussed with the Committee the various adverse events reported in the clinical trials, including the suicide-related events, during its December 15, 1992 meeting. None of the experts at the panel meeting concluded that Neurontin causes or increases the risk of these events and the panel voted unanimously in favor of FDA approval.

On December 30, 1993, after two years of review, the FDA concluded that Neurontin was safe and effective for its intended use and issued an approval letter. As of the time of approval in December 1993, FDA found that there was no scientific evidence supporting an increased risk of suicidal behavior and thinking with Neurontin and the agency did not include any such warning in the labeling.

In August 2001, Pfizer filed a supplemental new drug application for Neurontin seeking an indication for the management of neuropathic pain. Once again, the FDA analyzed all the

adverse events data, including reports of depression and suicide-related events from the clinical trials in neuropathic pain disorders. The FDA clinical reviewer with responsibility for the post-herpetic neuralgia ("PHN") application, Dr. Sharon Hertz, found that the incidence of treatment-emergent depression in the neuropathy studies was higher in patients on *placebo* than patients taking Neurontin (2.2% vs. 1.3%). With regard to suicidality, Dr. Hertz concluded that no suicide-related events were attributed to Neurontin.

Dr. McCormick, who reviewed the original Neurontin NDA and, by this time, was the Director of the FDA's Division of Anesthetic, Critical Care, and Addiction Drug Products, noted in her "Review and Basis for Approval Action," that "Neurontin had in 2002 been in use throughout the world for nearly a decade and had not given rise to a safety signal involving any psychiatric adverse event or suicidality." On May 24, 2002, FDA issued an approval letter for the treatment of PHN. FDA again conditioned approval on the verbatim use of the FDA-approved labeling and warnings. As with the prior approved labeling, FDA did not require warnings that Neurontin causes or increases the risk of suicide-related events.

On April 26, 2004, FDA asked Pfizer to perform a comprehensive search, pursuant to specific FDA-mandated protocols, of the Neurontin clinical trial and postmarketing data for cases of suicide and suicide attempt. Pfizer responded to FDA's request by filing two submissions, in September and November 2004, respectively. The September 2004 submission included the results of the search for cases of suicide and suicide attempts in 92 Phase 2-4 placebo-controlled, non-placebo controlled, and open-label (uncontrolled) Neurontin studies included in the investigational new drug applications ("INDs"), NDAs, and supplemental new drug applications ("sNDAs"), as well as the analysis of postmarketing data. These studies included patients with psychiatric disorders such as bipolar disorder, panic disorder, and social phobia.

The November 2004 submission included 55 Phase I Neurontin clinical trials in healthy volunteers and patients. There were no cases of suicide or suicide attempt in any placebo-controlled or non-placebo controlled studies in healthy volunteers or patients.

On October 20, 2005, after a review of the September and November 2004 submissions, the FDA asked Pfizer to make minor labeling changes to the terminology in the Adverse Reactions section of the Neurontin label regarding suicide-related events. The FDA did *not* find that Neurontin increased the risk of suicide-related events and, accordingly, did not ask Pfizer to add any warning whatsoever to the label, let alone a warning relating to suicide. On May 3, 2006, the FDA once again approved the Neurontin label *without* a suicide warning.

Thus, not only did the FDA determine that the Neurontin label in 2004 was adequate, the FDA gave further consideration to the Neurontin label based upon data available at the time of Mr. Smith's death or shortly thereafter and, once again, concluded that a suicide warning was not required.

Defendants submitted the results of controlled studies to the FDA in 1992, 2000, and 2002, and 2006. None of it supported an association between Neurontin and either suicide or suicidal behavior. Data from randomized controlled clinical trials data submitted to the FDA in 1992 showed that depression occurred in 1.1% of placebo-treated patients and in 1.8% of

Neurontin-treated patients – statistically equivalent results. Over 98% of test patients in this study had *no* suicidal thoughts or actions. Analysis of all "psychobiologic" events from randomized controlled clinical trials revealed a higher rate of occurrence of these events in the placebo-treated patients (9.0%) than in Neurontin-treated patients (8.3%). Similarly, randomized controlled clinical data submitted to the FDA in 2002 showed that patients on placebo had a higher rate of depression (2.2%) than patients taking Neurontin for pain (1.3%).

Analysis of 49 Neurontin randomized, controlled clinical trials in 2006 also demonstrated no association between Neurontin and suicidal behavior.[1] In these randomized controlled trials, which included 8,829 patients (5,194 of whom were treated with Neurontin), there were no completed suicides, no attempted suicides, and no preparatory acts toward imminent suicidal behavior in any patients taking Neurontin. Suicidal ideation was reported in two of 5,194 Neurontin-treated patients (0.039%) and one of 2,682 placebo patients (0.037%), statistically indistinguishable rates.

Plaintiff's experts rely upon a *pooled* meta-analysis by the FDA of clinical trial data for eleven different anti-epileptic drugs ("AEDs"), which resulted in the 2008 FDA Alert and, ultimately, the 2008 revised class-wide AED warnings on suicidal events. But Pfizer obviously did not possess such data on other AEDs, from which both the FDA and Plaintiff's experts have extrapolated, prior to the FDA Alert, much less in 2004, at the time Neurontin was last prescribed to and allegedly taken by Mr. Smith. Indeed, Plaintiff's claims pre-date, by many years, the FDA Alert and meta-analysis, on which Plaintiff's experts' opinions, and the revised FDA warning, are based.

In the absence of any epidemiologic evidence, Plaintiff's experts rely upon anecdotal adverse event data to support their argument that a suicide warning should have been included on the Neurontin label in 2004. However, as numerous courts and the FDA have recognized, adverse event data are unreliable and lack probative value on the issue of causation. In this case, the adverse event reports upon which Plaintiff relies are especially problematic. First, most of the data that Plaintiff relies upon consists not of reported suicides or suicide attempts, but other mood disorders, such as depression. The background rate of suicides and mood disorders among the population for which Neurontin is prescribed (which includes people suffering from seizures and chronic pain) is high. As a result, and as the FDA has made clear, meaningful conclusions about causation can only be drawn from controlled, epidemiologic evidence. As discussed above, such studies do not support a causal association between Neurontin and suicidal behavior. They certainly did not support such an association in 2004.

Neurontin Is Not Causally Associated With Suicidal Behavior Or Thoughts. As part of her burden to prove cause-in-fact, Plaintiff must prove, by a preponderance of the evidence, that Neurontin causes suicidal behavior or thoughts – commonly referred to as generic causation. However, as discussed above, Neurontin has been studied for many years, in several randomized, controlled, clinical studies – the gold standard of epidemiologic studies. In none of these studies was a statistically significant association between Neurontin and suicidal behavior observed. In

[1] Pfizer compiled such data in response to a request from the FDA and submitted it to the FDA in June 2006. The analysis used FDA-specified analytical criteria for evaluating suicidality.

their attempt to support their theory of causation, Plaintiff's experts rely upon (1) adverse event reports, (2) arguments regarding biological plausibility based upon their assertion that Neurontin is "gabaergic," and (3) the FDA's 2008 meta-analysis. None supports generic causation.

As a threshold matter, and as discussed above, it is clear, that causation cannot be established by adverse event reports. Plaintiff argues that the adverse event reports relied upon by her experts include dechallenge and rechallenge reports; however, dechallenge and rechallenge reports still constitute case reports and lack the statistical power to permit conclusions regarding causation. Moreover, such reports cannot eliminate chance as a cause of the onset or remission of symptoms – particularly symptoms endemic in the population at issue, such as the waxing and waning of depressive symptoms or suicidal ideation.

The theories offered by Plaintiff's experts regarding Neurontin's mechanism of action are likewise flawed. Initially, biological plausibility is not, itself, evidence of causation. Rather, it is one of the Bradford-Hill criteria that is used to test causation only *after* an association has been shown through competent epidemiologic evidence. No such association can be shown in this case. Further, Plaintiff's theory relies upon *in vitro* and animal studies, which many courts have recognized are unreliable evidence of causation. Studies conducted on humans do not support Plaintiff's theory that gabapentin reduces serotonin.

Finally, there is no epidemiologic evidence sufficient to permit a jury to find in Plaintiff's favor on the issue of generic causation. Significantly, this is not a case where there is an absence of epidemiologic data. Neurontin has been studied for many years, in several randomized, controlled, clinical studies – the gold standard of epidemiologic studies. As even Plaintiff's experts concede, in none of these studies was a statistically significant association between Neurontin and suicidal behavior observed.

The only epidemiologic evidence that Plaintiff has offered to counter the Neurontin randomized clinical trial data is the FDA's meta-analysis on antiepileptic drugs (AEDs) in 2008. However, the reliability of the FDA's meta analysis on the issue of causation (as opposed to a regulatory tool by which to guide FDA) policy is substantially undermined by the fact that the FDA pooled data from eleven different drugs with different pharmacologic properties, chemical structures, mechanisms of action and safety profiles. The FDA did not find – and openly acknowledged that it did not find – a statistically significant risk increase for Neurontin. While there was a statistically significant risk increase for the 11 different AEDs taken as a group, only 2 of the 11 – neither of them Neurontin – had a statistically significant increase. Significantly, even though the two drugs with an increase (lamotrigine and topiramate) accounted for only 38 percent of the total data, 61 percent of all of the suicidality events (thoughts and behaviors) observed in the entire meta-analysis came from the studies of these two drugs. Even more importantly, the FDA pooled data is inconsistent with Neurontin specific data.

Indeed, the FDA has made no factual determination that Neurontin causes or is associated with suicidality. The FDA made a finding of fact that the group, collectively, was associated with increased suicidality. The FDA acknowledged significant differences among the 11 AEDs it studied and made clear that it could make no findings of fact as to the individual drugs. The FDA then made a policy decision to treat all AEDs – including AEDs that were not

even part of the study and for which the FDA had no relevant data – as if the group finding had been made with respect to each AED.

Plaintiff Cannot Prove Specific Causation. Even if Plaintiff could produce evidence sufficient to meet her burden as to generic causation, she must also prove specific causation; i.e, that the absence of a suicide warning on Neurontin's label was a cause-in-fact of Mr. Smith's suicide. To do so, Plaintiff must prove that (1) Mr. Smith's physicians would not have prescribed Neurontin had its label contained a suicide warning, (2) that Mr. Smith actually ingested Neurontin sufficiently close in time to his suicide to make a threshold showing of biological plausibility necessary to support causation, and (3) that Mr. Smith's suicide was caused by his ingestion of Neurontin and not by his numerous other risk factors for suicide. The evidence does not support Plaintiff's claims of specific causation.

Plaintiff will be unable to prove that Mr. Smith's treating physicians would not have prescribed Neurontin to Mr. Smith had its label contained a suicide warning. The only Neurontin prescription Mr. Smith filled or took was written by Dr. Edward Mackey on March 9, 2004, who gave Mr. Smith a thirty-day prescription to treat his chronic pain. Dr. Mackey continues to prescribe Neurontin to this day. When asked whether he would have prescribed Neurontin to Mr. Smith based on the information he has today, Dr. Mackey testified only that he would prescribe Lyrica if Mr. Smith walked into his office on the date of his deposition. Lyrica, which was not available in 2004, is an AED that contains the same suicide warning mandated by the FDA for all AEDs. The fact, therefore, that Dr. Mackey continues to prescribe Neurontin today and would prescribe Lyrica, a drug containing the same suicide warning as Neurontin, to Mr. Smith negates any assertion that a suicide warning would have changed his decision to prescribe Neurontin to Mr. Smith in 2004.

Any argument by Plaintiff that an additional warning on Neurontin's label might have led to increased monitoring sufficient to prevent Mr. Smith's suicide is pure speculation. It is undisputed that Mr. Smith was depressed and suicidal long before he ever allegedly took Neurontin. Thus, given his numerous risk factors, Mr. Smith should have been monitored for suicidal behavior regardless of whether he was taking Neurontin.

In addition, there is insufficient evidence that Mr. Smith ingested Neurontin sufficiently close in time to his suicide for there to even be a possible causal association. As Plaintiff's expert Dr. Maris has conceded, the relevant time period for Mr. Smith's ingestion of Neurontin is narrow: Because Neurontin has a half life of 5 to 7 hours, there would be no appreciable Neurontin left in an individual's system within twenty-four hours after taking the drug. While Plaintiff's expert have suggested that Neurontin could have a continuing influence on neurotransmitters even after it was eliminated from an individual's system, neither of Plaintiff's experts provided any support for this speculative opinion, which was not contained in their Rule 26 reports. Neither has explained how long Neurontin purportedly affects brain chemistry, what dose would be required, or whether Mr. Smith had taken a sufficient dose to cause any such prolonged effect.

No one has testified that they observed Mr. Smith take Neurontin within any of the four days – let alone twenty-four hours – leading up to his suicide, or even on any day in particular. Plaintiff's experts do not know when Mr. Smith last took Neurontin prior to his death or how

many Neurontin pills Mr. Smith may have ingested at any time. Further, there is no toxicological evidence of any Neurontin in Mr. Smith's body at the time of his death. In sum, there is no direct evidence that Mr. Smith ingested Neurontin during the critical time period leading up to his death.

Rather than producing evidence of Mr. Smith's alleged ingestion of Neurontin, Plaintiff relies on her belief that Mr. Smith must have taken his medications as prescribed because "that was just the way he did things." Plaintiff's testimony is both speculative and contradicted by the facts. Mr. Smith had a prior history of non-compliance with Neurontin prescriptions. He had been prescribed Neurontin on May 5, 2003, by Dr. Paul McCombs, but it is undisputed that he did not fill, let alone take, this prescription. Likewise, Mr. Smith was given Neurontin samples in blister packs by Nurse Pamela Krancer, but it is undisputed that none of these blister packs were ever opened. It is likewise undisputed that Mr. Smith did not take his last prescription of Neurontin as directed. Had he done so, he would have run out of pills by April 8, but the bottle was "full" at the time of his death on May 13, 2004.

Plaintiff further relies on the deposition testimony of Mr. Smith's son-in-law, Lewis Wesley Carnahan II, regarding hearsay statements purportedly made by Mr. Smith on or about May 8, 2004, to the effect that he had taken Neurontin and that it had made him feel "loopy," as well as a May 19, 2004, letter written by Mr. Smith's dentist that recounts hearsay statements purportedly made by Mr. Smith more than a week earlier, on May 10, 2004. Defendants object to such evidence as hearsay, but, in any event, Mr. Smith's purported statements to Mr. Carnahan and Dr. Wood did not indicate that he had actually taken Neurontin on the days he made those statements, nor are they evidence that he took Neurontin during any of the following days leading up to his death. If anything, the assertion that Mr. Smith, in a three-day period, complained to two different people that Neurontin made him feel strange and was not helping him undermines, rather than supports, Plaintiff's speculation that he continued taking it.

Mr. Smith's Suicide Was Caused By Factors Unrelated To Neurontin. For more than ten years prior to his death, Mr. Smith suffered from chronic joint and spine abnormalities that caused him severe pain and required numerous replacement surgeries. The severe, unrelenting, chronic pain experienced by Mr. Smith continued up until his suicide. In May 2003, after undergoing spinal surgery, Mr. Smith stated that he "wished he could die because of pain and depression." He was then diagnosed with anxiety and depression and treated with Lexapro, an anti-depressant. Mr. Smith was twice referred for psychological evaluations, but he did not heed these referrals. According to Mr. Smith's daughter, Mr. Smith again contemplated suicide on March 1, 2004. Mr. Smith started to have trouble sleeping because of his increasing pain, and the Smiths began sleeping in separate bedrooms because of his restlessness.

During April and May of 2004, Mr. Smith's pain was "excruciating." He spent most of the day "lying around" because of pain. By this time, several surgeons had concluded that he was not a candidate for further surgical intervention. In a handwritten note, Mr. Smith stated that his doctors had "nothing to offer him" besides steroid injections, medication, and physical therapy, none of which eased his pain.

Three days before committing suicide, Mr. Smith told Dr. Wood, his dentist and longtime family friend, that an end to his pain seemed "hopeless." Mr. Smith told Dr. Wood that he had

tried to get second opinions regarding his back, but that every physician he saw seemed to tune him out after hearing he already had surgery. According to Mr. Smith, "[i]t was like they were all protecting each other." Mr. Smith told Dr. Wood that he wished he never had back surgery and that "now I am almost useless," because he could no longer do things he enjoyed, like cutting the grass. On May 13, 2004, Mr. Smith committed suicide. He left a suicide note that stated: "Pain has taken over my mind and body! I need back surgery, left and right rotator cuffs, right bicep torn, back surgery to correct pain in legs. Forgive me; I cannot go on like this. I cannot have my body, the temple of the Holy Spirit, cut on anymore. I have talked to God all night and he understands."

For the reasons stated in Defendant's prior motion to exclude the testimony of Plaintiff's experts Dr. Maris and Dr. Trimble (MDL R. 1629), the testimony of Plaintiff's experts is unreliable and cannot exclude alternative causes for Mr. Smith's suicide. In addition, the testimony of Defendant's experts will show that Mr. Smith's suicide is fully explained by his risk factors that pre-dated his use of Neurontin and that Neurontin was not a substantial contributing cause of his death.

Plaintiff Cannot Prove Proximate Cause. In addition to proving that that absence of a suicide warning was a cause-in-fact of Mr. Smith's suicide, Plaintiff must also prove that it was the proximate cause of his death. Tennessee courts have repeatedly recognized that suicide constitutes an independent intervening cause defeating proximate cause in most wrongful death actions. Recognizing that suicide is a willful act, Tennessee has long held that "[a]n act of suicide resulting from a moderately intelligent power of choice, even though the choice is determined by a disordered mind, should be deemed a new and independent . . . cause of the death that immediately ensues." *Jones v. Stewart*, 183 Tenn. 176, 179, 191 S.W.2d 439, 440 (Tenn. 1946). Thus, Tennessee law recognizes, as a matter of public policy, that someone should not be held liable for the volitional act of another person. *See Jones*, 183 Tenn. at 179, 191 S.W.2d at 440.

There are only three exceptions to the rule that suicide breaks the chain of causation, only one of which is even arguably applicable here: "where defendant's negligence causes 'delirium' or 'insanity' that results in self-destructive acts." *MacDermid v. Discover Fin. Servs.*, 488 F.3d 721, 736 (6th Cir. 2007). Here, the evidence does not support application of this exception but, instead, demonstrates that Mr. Smith understood the nature of his act.

2. Defenses

Without assuming the burden of proof of such defenses that they would not otherwise have, Defendants affirmatively assert the following defenses:

a) Plaintiff's claims are barred, in whole or in part, by the Supremacy Clause of the United States Constitution, Article VI, clause 2, and the laws of the United States because Defendants' product is comprehensively regulated by the United States Food and Drug Administration ("FDA") pursuant to the Federal Food, Drug & Cosmetic Act, 21 U.S.C. §§ 301 et seq. ("FDCA"), and regulations promulgated thereunder, and Plaintiff's claims conflict with the FDCA, with the regulations promulgated by FDA to implement the FDCA, with the purposes and objectives of the FDCA and FDA's implementing regulations, and with the specific

determinations by FDA specifying the language that should or should not be used in the labeling accompanying the drug.

b) Plaintiff's claims are barred, in whole or in part, by the deference that common law gives to discretionary actions by FDA under the FDCA.

c) Plaintiff's claims may be barred, in whole or in part, under the doctrine of primary jurisdiction, in that the pertinent conduct of Defendants and all their activities with respect to the subject product have been and are conducted under the supervision of the FDA.

d) The claims set forth in the Complaint are barred because the alleged injuries and damages, if any, were actually or proximately caused by the intervening or superseding conduct of persons or entities over which or whom Defendants had no control.

e) The alleged injuries and damages, if any, were due to idiosyncratic reactions to Neurontin for which Defendants cannot be held responsible. The claims set forth in the Complaint are barred because the alleged injuries and damages, if any, were caused by medical conditions or processes (whether pre-existing or contemporaneous) unrelated to Neurontin.

f) The claims set forth in the Complaint are barred by the learned intermediary doctrine.

g) Plaintiff's claims are barred under Section 402A, comments j and k of the Restatement (Second) of Torts and Sections 4 and 6 of the Restatement (Third) of Torts: Products Liability.

h) The claims set forth in the Complaint are barred because the methods, standards and techniques used in formulating Neurontin and in issuing warnings and instructions about its use conformed to the generally recognized, reasonably available and reliable state of knowledge in the field at the time Neurontin was manufactured.

i) The claims set forth in the Complaint are barred because the foreseeable therapeutic benefits of Neurontin outweighed any foreseeable risks of harm.

j) Plaintiff's breach of warranty claims are barred by the Uniform Commercial Code as enacted in Tennessee.

k) Plaintiff's claims are barred in whole or in part by the First Amendment to the United States Constitution.

l) To the extent Plaintiff's claims are based on alleged misrepresentations or omissions made to the FDA, such claims are barred pursuant to *Buckman Co. v. Plaintiff's Legal Committee*, 531 U.S. 341 (2001).

m) Plaintiff's breach of warranty claims are barred because: (i) Defendants did not make any express warranties to Plaintiff or Plaintiff's decedent;

(ii) Defendants' Neurontin advertisements and promotions were not an affirmation of fact or a promise made by the seller to the buyer that related to the drug Neurontin and became part of the basis of the bargain in connection with purchases of Neurontin made by Plaintiff or Plaintiff's decedent; (iii) Defendants' Neurontin advertisements and promotions were not a description of the drug included in any contract that was part of the basis of the bargain in connection with purchases of Neurontin made by Plaintiff or Plaintiff's decedent, such that a warranty was created that the drug would conform to the description; (iv) Plaintiff and Plaintiff's decedent did not read, see or hear about the alleged illegal "off-label" promotions; (v) there was a lack of privity between Defendants and Plaintiff and Plaintiff's decedent; and (vi) notice of an alleged breach was not given, or timely given, to the seller or Defendants.

n) Defendants assert every defense available under the Uniform Commercial Code, as enacted in Tennessee, found at Tenn. Code. Ann. § 47-1-101, et seq., and specifically including, but not limited to, Tenn. Code. Ann. § 47-2-103 - Definitions and Index of Definitions; Tenn. Code. Ann. § 47-2-313 - Express Warranties by Affirmation, Promise, Description, Sample; Tenn. Code. Ann. § 47-2-314 - Implied Warranty - Merchantability - Usage of Trade; Tenn. Code. Ann. § 47-2-315 - Implied Warranty - Fitness for a Particular Purpose; Tenn. Code. Ann. § 47-2-316 - Exclusion or Modification of Warranties; Tenn. Code. Ann. § 47-2-607 - Effect of Acceptance - Notice of Breach - Burden of Establishing Breach After Acceptance - Notice of Claim or Litigation to Person Answerable Over; Tenn. Code Ann. § 47-2-709 - Action for the price; Tenn. Code. Ann. § 47-2-714 - Buyer's Damages for Breach in regard to Accepted Goods; and Tenn. Code. Ann. § 47-2-715 - Buyer's Incidental and Consequential Damages.

o) Plaintiff is not entitled to an award of attorney fees and costs.

p) Plaintiff's claims are barred, in whole or in part, because Defendants did not make any false, misleading, or deceptive statements to Plaintiff or Plaintiff's decedent in their advertisements and/or promotional materials concerning Neurontin. As to any statement asserted against Defendants that Plaintiff alleges to be false, misleading, or deceptive, Defendants had no reasonable grounds to believe, and did not believe at the time such a statement was made, that the statement was false, misleading, or deceptive.

q) The alleged injuries and damages, if any, were caused by the acts or omissions of Plaintiff's decedent, and/or by his fault. Any recovery might be reduced accordingly or eliminated altogether.

r) Plaintiff's cause of action is barred in whole or in part by lack of defect, as any product allegedly ingested by Plaintiff's decedent was properly prepared in accordance with the applicable standard of care.

s) Defendants and Neurontin were in compliance with legislative regulatory standards and/or administrative regulatory safety standards relating to design, performance, warnings and/or instructions and, therefore, Neurontin is deemed not defective.

t) Plaintiff's claims are barred by the "state of the art" defense. Neurontin, when placed into the stream of commerce, was a reasonably safe and effective

prescription drug in light of the then existing and reasonably available scientific, medical, and technological knowledge. To the extent Plaintiff claims that Neurontin was dangerous or defective in certain respects, Defendants state that any such risks associated with Neurontin were not known and could not reasonably be discovered at the time the product was placed into the stream of commerce.

u) To the extent it is determined that Defendants contributed to the Plaintiff's damages, if any, Defendants specifically assert the doctrine of modified comparative fault, as adopted in Tennessee.

v) Defendants assert every defense available under the Tennessee common law of product liability and the Tennessee Products Liability Act of 1978, as amended, and found at Tenn. Code. Ann. § 29-28-101 et seq., specifically including, but not limited to, Tenn. Code. Ann. § 29-28-102 - Definitions; Tenn. Code. Ann. § 29-28-103 - Limitations of Actions; Tenn. Code. Ann. § 29-28-104 - Compliance with Governmental Standards - Rebuttable Presumption; Tenn. Code. Ann. § 29-28-105 - Determination of Defective or Dangerous Condition; Tenn. Code Ann. § 29-28-106 – Seller's Liability; Tenn. Code Ann. § 29-28-107 Complaint - Statement of Damages; Tenn. Code. Ann. § 29-28-108 - Product Altered or Abnormally Used.

w) The Complaint fails to state facts sufficient to sustain a claim for, or recovery of, punitive or exemplary damages.

x) Plaintiff's claims for punitive and exemplary damages are barred by the Fourth, Fifth, Sixth, Eighth, and Fourteenth Amendments to the United States Constitution and applicable state law.

y) With respect to Plaintiff's demand for punitive and exemplary damages, Defendants specifically incorporate by reference any and all standards or limitations regarding the determination and enforceability of punitive and exemplary damage awards that arose in the decisions of *BMW of North America Inc. v. Gore*, 517 U.S. 559 (1996), *Cooper Industries, Inc. v. Leatherman Tool Group*, 532 U.S. 424 (2001), *State Farm Mut. Auto. Ins. Co. v. Campbell*, 538 U.S. 408 (2003), and *Philip Morris USA v. Williams*, 549 U.S. 346 (2007).

V. Contested Issues Of Law

A. Plaintiff's Contested Issues Of Law

1. Whether Defendants were negligent with respect to the research and development of Neurontin in the manner in which they investigated or tested the association between Neurontin and suicidality.

2. Whether Defendants failed to adequately warn doctors and patients of risks of suicidality that Defendants knew or should have known were associated with taking Neurontin for off-label uses.

3. Whether Defendants failed to adequately monitor the effect of Neurontin on patients taking the drug after Neurontin was approved by the FDA and entered the marketplace.

4. Whether Neurontin is defective as marketed or otherwise.

5. Whether Neurontin causes depression and suicidality in some patients.

6. Whether Defendants had a duty to disclose the depressive and suicidal side effects of Neurontin when they knew of Neurontin's substantial off-label usage.

7. Whether Defendants had a duty to disclose to prescribing physicians how Neurontin works (e.g., its "mechanism of action") so that prescribing physicians could perform a risk-benefit analysis when prescribing Neurontin and could carefully monitor its results.

8. Whether Defendants withheld medical and scientific data regarding psychobiologic side effects, including depression and suicidality, by concealing the information from the medical community and consumers, including Richard Smith and his medical providers.

9. Whether Defendants intentionally withheld material information about the side effects of Neurontin from both consumers and their prescribing physicians with the intent to deceive.

10. Whether Defendants breached their duty to disclose to physicians and patients material facts about the risks of psychobiologic side effects, including depression and suicidality, with Neurontin use.

11. Whether Defendants breached their duty to disclose that Neurontin had an association with adverse psychobiologic effects, such as depression and suicidality, in its details to doctors' offices.

12. Whether Defendants breached their duty to disclose that Neurontin had an association with adverse psychobiologic effects, such as depression and suicidality, in its product labeling and package inserts.

13. Whether Defendants failed to exercise reasonable care to warn of the risks of Neurontin.

14. Whether Defendants' conduct was a substantial factor, also known as a proximate cause, of Richard Smith's injuries and death.

15. Whether Richard Smith's wife, Ruth Smith, and children, suffered a loss of consortium, loss of services, and other damages, as a result of Richard's death.

16. The amount in dollars of damages incurred in the past and future that should be awarded to Richard Smith's wife and children.

17. Whether punitive damages should be assessed as a result of Defendants' actions or failure to act, and if so, the amount of punitive damages to be awarded.

18. The admissibility of any other evidence objected to by Plaintiff's objections to Defendants' exhibit and deposition designations.

Issues numbered "1"-"17" are for the jury. Issue numbered "18" is for the Judge.

B. Defendant's Contested Issues of Law[2]

1. Whether Pfizer had a legal duty at any time May 13, 2004 to warn physicians of any alleged risk of suicide or suicidal behavior associated with Neurontin. (Mixed question of law and fact for the Court and jury.)

2. Whether Plaintiff's expert testimony on the issue of generic causation satisfies the requirements of *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), and Federal Rules of Evidence 702 and 703. (For the Court.)

3. Whether Plaintiff's expert testimony on the issue of specific causation satisfies the requirements of *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), and Federal Rules of Evidence 702 and 703. (For the Court.)

4. Whether Plaintiff's expert testimony on the issue of pharmacovigilence and duty to warn satisfies the requirements of *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), and Federal Rules of Evidence 702 and 703. (For the Court.)

5. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find that the Neurontin warning provided to physicians in 2004 was inadequate or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

6. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find that the Neurontin can cause suicide or suicidal behavior or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

7. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find that the Neurontin caused Richard Smith's death or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

8. Whether the absence of a suicide warning on the Neurontin label in 2004 was a cause-in-fact of Mr. Smith's suicide. (For the jury.)

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[2] To the extent that this Court or the MDL Court have ruled on questions of law stated herein, they are included in order to preserve them for reconsideration by the Court prior to entry of judgment or for appeal.

9. Whether the absence of a suicide warning on the Neurontin label in 2004 was a proximate cause of Mr. Smith's suicide. (Mixed question of law and fact for the Court and the jury.)

10. Whether the damages sought by Plaintiff in this action are legally compensable under the Tennessee wrongful death statute. (For the Court.)

11. Whether loss of parental consortium is recoverable in a suit brought by a surviving spouse under the Tennessee Wrongful Death statutes. [See D.E. 104, 105]. (For the Court.)

12. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find that the Defendants are liable to Plaintiff for compensatory damages or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

13. Whether Defendants are liable to Plaintiff for compensatory damages. (For the jury.)

14. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find that the Defendants are liable to Plaintiff for punitive damages or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

15. Whether clear and convincing evidence supports an award of punitive damages in this case. (For the jury.)

16. Whether the imposition of punitive damages on the facts of this case is constitutionally permissible or whether judgment should be entered as a matter of law in favor of Defendants. (For the Court.)

17. Whether the amount of any award of punitive damages on the facts of this case is constitutionally permissible. (For the Court.)

18. Whether Plaintiff's claims are barred, in whole or in part, by federal law or preemption. (For the Court.)

19. Whether Plaintiff failed to proved the required pre-suit notice for her breach of warranty claims. (For the Court.)

20. Whether Plaintiff's claim for breach of the implied warranty of fitness fails because neither Mr. Smith nor Dr. Mackey actually relied on Pfizer's skill and judgment in purchasing Neurontin. (Mixed question of law and fact for the Court and jury.)

21. Whether Pfizer breached the implied warranty of merchantability. (For the jury.)

22. Whether Pfizer breached the implied warranty of fitness for a particular purpose. (For the jury.)

23. Whether any breach of warranty, if found by the jury, was a cause-in-fact of Mr. Smith's suicide. (For the jury.)

24. Whether any breach of warranty, if found by the jury, was a proximate cause of Mr. Smith's suicide. (Mixed question of law and fact for the Court and the jury.)

25. Whether Plaintiff's claim for fraudulent concealment is legally cognizable under Tennessee law. (For the Court.)

26. Whether Defendants fraudulently concealed relevant information regarding Neurontin from the Decedent's prescribing physicians. (For the jury.)

27. Whether any fraudulent concealment, if found by the jury, was a cause-in-fact of Mr. Smith's suicide. (For the jury.)

28. Whether any fraudulent concealment, if found by the jury, was a proximate cause of Mr. Smith's suicide. (Mixed question of law and fact for the Court and the jury.)[3]

29. Whether there is a legally sufficient evidentiary basis for a reasonable jury to find for the Plaintiffs on the issues stated in questions 20 through 28. (For the Court.)

30. The issues raised by Defendants' motions in limine and objections to Plaintiffs' exhibits and deposition designations.

VI. Known Evidentiary Disputes

1. The issues raised by Plaintiff's Motions in Limine.

2. The issues raised by Defendants' Motions in Limine.

3. The issues raised by Plaintiff's objections to Defendants' exhibit list, attached as Exhibit A.

4. The issues raised by Plaintiff's objections to Defendants' deposition designations, attached as Exhibit B.

5. The issues raised by Defendant's objections to Plaintiff's exhibit list, attached as Exhibit C.

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[3] Defendants submit issues 20 through 28 in order to preserve them; however, Defendants respectfully submit that, even if legally cognizable, Plaintiffs' breach of warranty and fraudulent concealment claims are redundant of her product liability claims for failure to warn. As a result, they should not be independently submitted to the jury, because to do so creates the risk of juror confusion and inconsistent verdicts.

4. The issues raised by Defendants' objections to Plaintiff's deposition designations, attached as Exhibit D.

VII. Stipulations

The parties have reached a stipulation regarding authenticity of documents, which is being filed separately.

Entered this 30th day of April, 2010.

Aleta A. Trauger
U.S. District Judge

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